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APPLICATION NO.	09/701,437	FILING DATE	03/02/2001	FIRST NAMED INVENTOR	Thomas Charles Elleman	ATTORNEY DOCKET NO.	50179-086	CONFIRMATION NO.	9960
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20277 7590 09/22/2003

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EXAMINER

ALLEN, MARIANNE P

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 09/22/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary		Applicant(s) ELLEMAN ET AL.	
Application No. 09/701,437		Examiner Marianne P. Allen	
		Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

Status

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

☒ 1) Responsive to communication(s) filed on 21 July 2003.

☒ 2a) This action is FINAL.

☐ 2b) This action is non-final.

☐ 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

☒ 4) Claim(s) 1 and 54-75 is/are pending in the application.

☐ 4a) Of the above claim(s) _____ is/are withdrawn from consideration.

☐ 5) Claim(s) _____ is/are allowed.

☒ 6) Claim(s) 1 and 54-75 is/are rejected.

☐ 7) Claim(s) _____ is/are objected to.

☐ 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

☐ 9) The specification is objected to by the Examiner.

☐ 10) The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

☐ 11) The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

☐ 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

☐ 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

☐ 1. Certified copies of the priority documents have been received.

☐ 2. Certified copies of the priority documents have been received in Application No. _____.

☐ 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

☐ 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

☐ 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

☐ 1) Notice of References Cited (PTO-892)

☐ 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

☐ 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____

☐ 6) Other: _____

☐ 5) Notice of Informal Patent Application (PTO-152)

☐ 4) Interview Summary (PTO-413) Paper No(s) _____

DETAILED ACTION

Applicant's arguments filed 7/21/03 have been fully considered but they are not

persuasive.

Claims 2-53 have been cancelled. Claims 58-75 have been newly added. Claims 1 and 54-75 are under consideration by the examiner.

Claim Rejections - 35 USC § 101

Claims 1 and 58 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

To the degree that the method of claim 1 is directed to a completely *in silico* method where the obtaining and testing steps are computational in nature rather than laboratory chemistry (see claim 54 for example), the claims are considered to be non-statutory as they merely manipulate data. The results of the method as written do not provide a concrete, tangible, and useful result as all compounds are assessed, obtained (represented by a data structure), and tested. (See for example Wang et al. reference submitted by applicant as Exhibit E.)

Claim Rejections - 35 USC § 112

Claims 1 and 54-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1 has been amended to recite "modulates binding of a natural ligand" and to require testing the compound for its ability to modulate said binding. While page 7, lines 33-35,

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discloses preventing the binding of the natural ligand, the specification does not appear to contemplate or disclose the broader concept of modulating binding of natural ligands.

Claim 1 has been amended to recite "modulates signal transduction via the EGF receptor, ErbB2, ErbB3 or ErbB4" and to require testing the compound for its ability to modulate said signal transduction. No basis has been pointed to and none is apparent for this concept within the claimed method of identifying a compound.

Basis for new claim 57 was not seen on any of the pages pointed to by applicant.

Clarification is requested.

Should this new matter rejection be overcome, the claims would be subject to at least the following enablement rejection.

The specification does not exemplify modeling of any compound and a molecule as defined by claim 1(A)(i)-(iii). The specification does not disclose any compounds meeting the structural and functional limitations required by the claims. As written, the claim 1 recites the step of assessing the stereochemical complementarity between a compound and a recited molecule, obtaining the compound, and testing the compound. Note that the claims do not recite any scoring function or cut-off value to discriminate high-ranking compounds from low-ranking compounds. That is, the claims can be considered to be effectively no different from obtaining and testing all potential compounds as all assessed compounds will be obtained and tested. Note that claim 1(B) requires obtaining "a" compound and not "the" compound of (A). Likewise, claim 73 does not discriminate between compounds to be obtained and selected. Applicant's arguments indicate that all compounds will give a computational result for stereochemical complementarity even if it is poor.

In particular, claim 1, part (ii), recites using "one of more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations." The specification provides no guidance on how to do this or which subsets to use. The response refers to pages 5-6 which does not discuss whole body translations and/or rotations.

Furthermore, the specification does not clearly specify what is required to be performed in assessing "stereochemical complementarity." There does not appear to be a specific definition as to how applicant defines "stereochemical complementarity." Page 5, lines 12-15, discusses this in the context of a lock and key visualization with the cavity in the receptor site. Page 12, lines 20-35, discusses this in the context of matching intra-site surface coordinates lining the groove of the particular receptor site. Page 13, lines 7-9, discusses this in the context of

optimizing, geometrically or chemically, the "fit." The claims don't make clear which, if any, of these discussions of "stereochemical complementarity" are intended to be embraced by the claims. There are no limitations to cavities, binding sites, or energy optimization, for example. As such, one of ordinary skill in the art practicing the invention would not know what positive, active steps must be performed to meet these limitations. Applicant argues that there would have been programs known at the time of the invention for determining binding pockets. However, the claims do not require finding a binding pocket, using a known binding pocket, or using a docking program. The claims do not appear to be limited to these concepts.

Claims 1 and 54-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to recite "natural ligand." It is not known what the metes and bounds of this phrase are. It is not known what are considered to be natural ligands of the EGF receptor, ErbB3 or ErbB4 as set forth in the claim. For examples, are these ligands limited to those that bind *in vivo* in a natural biological setting or do they include any ligand that binds *in vitro*? Does this phrase exclude synthesized organic compounds?

Claim 1 has been amended to recite "signal transduction via the EGF receptor, ErbB2, ErbB3 or ErbB4." It is not known what the metes and bounds of this phrase are. For example, the claim could be construed as intending the signal transduction of the named receptors themselves or altering signal transduction of other receptors in a cascade including these receptors (either upstream or downstream of the named receptors). With respect to claims 70-72, it is not known what the increase, decrease, or inhibition in signal transduction is in comparison to or when this step occurs within the method of claim 1.

The claims continue to recite "substantially as shown" and "form an equivalent three-dimensional structure." These phrases are indefinite as set forth in the prior Office action. MPEP 2173.05(a) states that the meaning of every term used in a claim should be apparent from the prior art or from the specification at the time the application is filed. Neither the specification nor prior art of record specifically define these phrases. Applicant points to MPEP 2173.05(b) and points to Andrew Corp. v. Gabriel Electronics, 847 F.2d 819, 6 USPQ2d 2010 (Fed. Cir. 1988) in support of their assertion that these phrases are definite. This is not agreed with. MPEP 2173.05(b) states that acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. When a term of degree is presented in a claim, first a determination is to be made as to whether the specification provides some standard for measuring that degree. If it does not, a determination is made as to whether one of ordinary skill in the art, in view of the prior art and the status of the art, would be nevertheless reasonably apprised of the scope of the invention. However, the instant specification does not provide any standard for measuring what is "substantially as shown" or "an equivalent three-dimensional structure" and neither does the prior art. Applicant has provided no evidence that one of ordinary skill in the art would be apprised of the scope of "substantially as shown" and "form an equivalent three-dimensional structure." There does not appear to be an art understood definition of these phrases.

Claim 1 (A) refers to "the molecule." There is no antecedent basis in the preamble for a molecule.

Claim 62 is confusing in adding the step of modifying the compound. The claim does not make clear if this is performed before or after obtaining in step (B) or before or after testing in step (C). Is the compound modified as part of the modeling steps, that is choose a compound and modify the structure of the compound within the unspecified positive active steps for assessing stereochemical complementarity in (A) to meet the criteria set forth in claim 62? In addition, Figures 7, 8, and 9 are part of the model polypeptide fold of the L1 and S1 domains of the EGF receptor. The figures don't clearly show the amino acid residues intended to meet the limitation of "at the surface of the molecule lining a groove region." It is not known whether some particular amino region or some portion of this specific three dimensional structure was intended to be a limitation of this claim.

Claim 67 is confusing in adding the step of modifying the compound. The claim does not make clear if this is performed before or after obtaining in step (B) or before or after testing in step (C). Is the compound modified as part of the modeling steps, that is choose a compound and modify the structure of the compound within the unspecified positive active steps for assessing stereochemical complementarity in (A) to meet the criteria set forth in claim 67? Is the binding enhanced with respect to the unmodified compound or some other compound?

Claim 73 is unclear as to whether the K_d or K_i is a predicted, calculated, or experimentally determined value.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE

MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this

final action.

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666.

The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone number for the

organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Marianne P. Allen
Marianne P. Allen

Primary Examiner

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